REVIEW

Breathing retraining and exercise conditioning in patients with chronic obstructive pulmonary disease (COPD): a physiological approach

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Abstract In this review we shall consider the commonest techniques to reduce dyspnea that are being applied to patients with chronic obstructive pulmonary disease (COPD) subjected to a pulmonary rehabilitation program (PRP). Pursed lip breathing (PLB) and diaphragmatic breathing (DB) are breathing retraining strategies employed by COPD patients in order to relieve and control dyspnea. However, the effectiveness of PLB in reducing dyspnoea is controversial. Moreover, DB may be associated with asynchronous and paradoxical breathing movements, reflecting a decrease in the efficiency of the diaphragm. Exercise training (EXT) is a mandatory component of PRP. EXT has been shown to improve exercise performances and peripheral muscle strength. Recent studies have focused on the effect of EXT on breathlessness. However, concerns persist as to whether the decreased sensation of dyspnea for a given exercise stimulus is principally due to psychological benefits of rehabilitation or to improved physiological ability to perform exercise. The effect of EXT on breathlessness may be reinforced by inhaling oxygen. However, two studies have recently shown that breathing supplemental oxygen during training has either a marginal effect or no advantage over training. In a comprehensive PRP, strength training (ST) and arm endurance training (AET) could have a role in decreasing peripheral muscle weakness and metabolic and ventilatory requirements for AET. The role of unloading the respiratory muscles during EXT has to be clarified.

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Keywords pulmonary rehabilitation; dyspnea; COPD.

INTRODUCTION

One of the two major goals in the management of chronic obstructive pulmonary disease (COPD) is to decrease respiratory symptoms and improve the quality of life (QoL). As a result of pulmonary rehabilitation programs (PRP), improvements have been demonstrated in objective measures of QoL (1), well-being (2) and health status, including reduction of respiratory symptoms, increase in exercise tolerance and functional activities such as walking, enhanced ability of performing activities of daily living and improved psychological function (3,4).

Referral to a comprehensive pulmonary rehabilitation program is indicated in COPD patients who have been placed on optimal medical therapy and who: (1) continue to display severe respiratory symptoms, mostly breathlessness; (2) have had several emergency ward or hospital admissions per year; (3) exhibit limited functional status and restricted activities of daily living and (4) experience impairment in QoL (3,4).

PRPs are usually employed on an outpatient basis and comprehensive programs vary in their frequency and duration, with the optimal frequency and length remaining a matter of debate.

In this review, we shall consider the most common techniques to reduce dyspnea that are being applied to patients with COPD.

BREATHING RETRAINING (BR) AND BODY POSTURE

The goal of BR is to help the patient to relieve and control breathlessness and counteract abnormalities such as dynamic hyperinflation associated with COPD.

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Review of clinical studies evaluating the effects of BR indicate that improvement in clinical symptoms is a more consistent finding than any measurable impact on physiological parameters (3,4).

Pursed lip breathing (PLB)

PLB is a breathing retraining strategy often spontaneously and voluntarily employed by COPD patients in order to relieve and control dyspnea during exercise or daily activities or during periods of increased ventilatory demand (5,6). PLB improves gas exchange (5–8), decreases respiratory rate, increases tidal volume (5,7,9,10) and increases the activity of inspiratory and expiratory muscles that take over the activity of breathing (5). In circumstances of hyperinflation, an increased motor command to, and a reduced muscle strength of, the diaphragm are likely explanations for dyspnea (11). A deflationary activity on chest wall of PLB should potentially reduce breathlessness. However, the effectiveness of PLB in reducing dyspnea in COPD is controversial, with some studies demonstrating either decrease (5,8,12), no changes (13) or increase in breathlessness at rest (10) and during exercise (14). The fact that PLB does not promote any reduction in pulmonary volume and whether the self-imposed rhythmic respiration with PLB affects chest wall (CW) motion and compartmental coordinated activity have as yet to be demonstrated. By applying a 3-D optoelectronic plethysmograph (OEP), Nerini *et al*. (15) have recently shown a marked decrease in end expiratory lung volume (EELV), localized at abdominal level, a pattern never shown before. They have also confirmed previous data by Breslin (6) showing increase in expiratory muscle activity, and have extended those data in that abdominal muscle activity is greater than that derived from the mere measures of changes in end expiratory gastric pressure (P_{gae}).

Anecdotal evidence of impaired breathlessness with PLB has been reported in COPD patients (5,14). We speculate that this may in part be due to increased activity of the respiratory muscles aimed at avoiding overtaxing the diaphragm.

Leaning forward (LF)

Although this is not a part of PRP, it may help patients to relieve breathlessness. Standing position increases EMG of the diaphragm (E_{di}), lowers trans-diaphragmatic pressure (P_{di}) and increases E_{di}/P_{di} ratio. At variance, LF decreases EMG activity of many respiratory muscles (16), including the diaphragm, and improves E_{di}/P_{di} ratio (17). The reason for the association of LF with decrease in breathlessness lies in the common belief that breathlessness is linked to the increase in the central motor command to the respiratory muscles (18). Decrease in respiratory muscle activation lowers breathlessness.

Diaphragmatic breathing (DB)

The costal and crural parts of the muscle are electrically arranged partially in series and partially in parallel (19). With hyperinflation, costal and crural parts are arranged in parallel, a condition where: (1) the zone of apposition decreases; (2) the abdominal pressure (P_{ab}) no longer expands the rib cage (RC); (3) the system produces less pressure; (4) the diaphragm expands the abdomen but has a deflationary action on the RC. Thus, in patients with COPD DB may be associated with asynchronous and paradoxical breathing movements (20,21). A recent study by Gosselink *et al*. (22) showed that, compared to quiet breathing, with DB inspiratory abdominal volume (V_{ab}) increases while the volume of rib cage (V_{rc}) decreases. This is a paradoxical breathing reflecting the limitation of DB which decreases the efficiency of the diaphragm. In the same study, dyspnea tended to increase with DB. Recently similar results have been produced by Vitacca *et al*. (23) in hypercapnic patients with COPD. It is possible that patients with limited hyperinflation may benefit from DB while severely hyperinflated patients are incapable of performing DB (24).

Association of breathing retraining with body position is being commonly performed by patients to reduce dyspnea (3,4).

EXERCISE TRAINING (EXT)

EXT is a mandatory component of PRP. Patients with COPD should regularly perform aerobic lower extremity endurance exercises to enhance performance of daily activities and reduce dyspnea (3,4).

General exercise training

Patients experience increased capacity and endurance for exercise and physical activity after EXT even though lung function may remain unchanged (25–28). Recent studies have shown an early onset of lactic acidosis during exercise at high exercise levels in COPD patients (29–32). Improvements in maximal and submaximal exercise responses obtained after EXT at high exercise levels (30,32,33) indicate improved aerobic metabolism (30,32,33). The study by Casaburi *et al*. (30) showing the effects of sustained level of exercise on the delay in anaerobic threshold in COPD patients with moderate airway obstruction indicates that a physiological training response had occurred. Maltais *et al*. (32) have indicated a beneficial effect on skeletal muscle level as shown by the increase in lactate threshold, citrate synthase (CS) and 3-hydroxy-acyl CoA dehydrogenase (HADH). Reduction

in lactic acidosis was inversely related to changes in activity of CS and HADH. However, improvement in exercise capacity and oxidative enzyme activity of the peripheral muscles did not significantly relate to each other (32).

Cycloergometer training at 60–80% maximal work load has been shown to improve maximal work load and endurance time (30,32). Maltais *et al*. (33) have shown that the ability of patients to increase the training intensity ($\%W_{max}$) progressively increased over 6 weeks of training period and then plateaued at 60–65% of maximum work load (WL_{max}). Training duration also increased from 15 to 27 min. Importantly, WL($\%WL_{max}$) was independent of maximum O_2 uptake ($V_{O2\ max}$) (% predicted), age and baseline forced expiratory volume in 1 s (FEV_1). These results are consistent with and extend those of previous studies indicating that patients with severe COPD can improve their exercise tolerance after endurance training (29,30,34,35).

It should be noted that the feasibility of near-maximal high-intensity program lies upon the criteria used to define high intensity; the protocol used during the incremental exercise test can influence the WL_{max} achieved. The work rate for a given V_{O_2} should be greater when using larger work rate increments than when using smaller increase in work rate (36). This may be more important in COPD patients with low V_{O_2} kinetics during exercise (37).

In general, training strategies include walking, treadmill or cycling exercise, 3–5 weekly exercise sessions, for 6–12 weeks (30,32,38–43). However, there is as yet no consensus on the optimal training intensity prescription for patients with COPD (44). Although higher intensity training (60–80% of pre-training exercise capacity) seems to be of advantage (30), the effectiveness is likely to be related to the total amount of training performed (the product of training and duration). Furthermore, high-intensity training is associated with greater cardiovascular risk and orthopedic injury while possibly also decreasing compliance with the treatment program (45). In hypoxemic and hypercapnic COPD, the imposed load for 20–30 min is hardly tolerated. Interval training (2–3 min intensity 60–80% [WL_{max}]) has shown to elicit similar results as endurance training (46).

EXT has been shown to improve exercise performances and peripheral muscle strength (47,48). Beneficial effects have been obtained with treadmill walking exercise (38,43) and combined walking and cycling (42).

Casaburi *et al*. (41) have focused on the mechanism whereby EXT improves exercise tolerance in COPD (Fig. 1). On the other hand recent studies have focused on the effect of EXT on breathlessness. The disparity between the respiratory motor output and the mechanical response of the system is thought to play a major role in the increase perception of exercise dyspnea in COPD patients (49,50). Conflicting results, however, indicate the lack of relationship between dyspnea and any mechanical variable in exercising COPD (51). Therefore, concerns

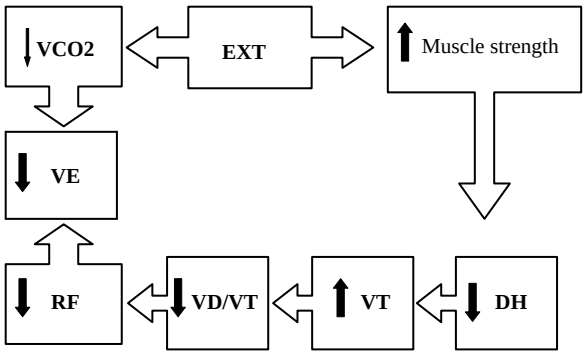

Fig. 1. Mechanism whereby exercise training programs (EXT) improve exercise tolerance in patients with COPD. EXT acts by increasing muscle strength with minimal decrease or unchanged CO_2 output (V_{CO_2}). Increase in muscle strength decreases dynamic hyperinflation (DH) thereby increasing tidal volume (V_T) and decreasing dead space (V_D) to V_T ratio (V_D/V_T). Decrease in respiratory rate (R_R) with the unchanged V_{CO_2} lower minute ventilation (V_E).

persist as to whether the decreased sensation of dyspnea for a given exercise stimulus is principally due to psychological benefits of rehabilitation or to improved physiological ability to perform exercise. The reduction of exercise dyspnea after EXT has been partially explained by reduced ventilatory requirement (VR) (41). However, in a lack of any improvement in operational lung volume, the arguments for reduced mechanical impedance as an explanation for the reduced VR remain speculative (41,52). On the other hand, it has been suggested that factors such as increased symptom tolerance are also likely to play an important role on the reduced exercise dyspnea post-EXT (42,53,54). In the study by O'Donnell *et al*. (42) EXT improved breathlessness, but for a given minute ventilation (VE) there was a greater improvement than that predicted indicating also that an increased symptom tolerance to sensory perturbations induces dyspnea.

More recently, O'Donnell *et al*. (47) have shown that general EXT improves strength and endurance of the peripheral leg muscles, decreases B_{org} and log effort (LE) but strength and endurance do not relate to either B_{org} or LE. So increased tolerance to stimuli or altered perceptual response to evoked sensation may also contribute to score symptom alleviation. Nonetheless, evidence of increased symptom tolerance associated with EXT should be provided after close evaluation of the mechanical factors involved in the coupling between respiratory motor output and mechanical response of the respiratory system (55).

Oxygen administration

The effect of EXT on breathlessness may be reinforced by inhaling oxygen. Administration of 30–60% oxygen

enhances ventilatory exercise performance in COPD (56–60). Casaburi *et al*. (30) have shown that decrease in VE was associated with decrease in lactate production. Inhaling 60% oxygen reduced lactate production and ventilation in COPD (60). As a consequence of the improved aerobic metabolism, breathlessness decreases at isowork load (58). Decrease in VE is the reason for decrease in breathlessness, particularly in patients with more severe degree of obstruction and hypoxemia (60). Former studies by Criner and Celli (61) with 30% oxygen administration had shown a change in the strategy of respiratory muscle recruitment whereby increase in diaphragmatic performance avoids overtaxing RC and accessory muscles and decreases breathlessness. Nevertheless, the effect of oxygen on breathlessness may occur independently from ventilatory changes indicating the role of central mechanism(s) on the perception of breathlessness (62). Two recent studies (63,64) have recently shown that breathing supplemental oxygen during training has either a marginal effect or no advantage over training while breathing room-air. Despite the evidence of short-term beneficial effects, there are no studies on long-term effects of oxygen on factors limiting effort tolerance and breathlessness in patients with COPD.

TRAINING TO STRENGTH AND ENDURANCE OF THE INSPIRATORY MUSCLES

Inspiratory muscle training (IMT) in addition to exercise training has been shown to improve exercise capacity more than exercise training alone (65–67). IMT as monotherapy was found to decrease dyspnea (67–69). Strength training may be obtained by maximum static inspiratory (MIP) and expiratory effort over vital capacity every 3–5 min for periods of 20–30 min a day. Alternatively, strength can be also increased by loading protocol involving inspiratory effort against flow resistive or threshold loads to generate target levels of peak inspiratory mouth pressure $>$ 33% MIP for 30–60 min daily for 5–7 days a week (69,70). The lack of improvement in MIP noted in some trials may be because of insufficient training intensity (71). Indeed, a recent meta-analysis has shown that overall exercise endurance improved in studies of ventilatory muscle training in which the training stimulus led to an increase in MIP but did not improve in the studies without improvements in respiratory muscle strength following training (72).

Endurance and the sense of respiratory effort depend on pressure, inspiratory flow, inspiratory time (T_i), and the ratio of T_i to the total time of the respiratory cycle (T_{tot}), and R_f (73). It seems probable that subjects breathing spontaneously on a given resistance may vary their inspiratory flow rate decreasing the sense of respiratory effort by reducing peak inspiratory pressure (P_i), or the pressure time index (PT_i), i.e., the area under the pressure–time curve of the inspiratory muscles. In this way, peak intra-thoracic pressure and PT_i may be similar with and without resistance. In other words, resistive breathing has the disadvantage that inspiratory pressure is flow-dependent. For training to have consistent effects on endurance, patients have to be coached to breathe with longer T_i and lower peak pressure such that PT_i is greater than during spontaneous breathing (74). In that study, while peak mouth pressure was higher during spontaneous breathing, PT_i was appreciably greater during coached breathing. After a training period of 10 weeks maintaining PT_i at 25%, $P_i/P_{i\ max}$ at 50% and T_i/T_{tot} at 50%, Criner *et al*. (75) found an increase in trans-diaphragmatic (P_{di}) twitch of about 40%. Breathing on resistance loads at high respiratory rate increases strength and endurance in a small number of COPD patients.

Unlike resistive breathing, isocapnic hyperventilation (70–90% maximum voluntary ventilation (MVV)) for periods of 15-min a day 6 times per week (76,77) is associated with lower levels of pressure but greater inspiratory flow and probably a greater extent of muscle shortening. Thus, isocapnic hyperventilation increases velocity of shortening at low level of pressure or tension (78). Like isocapnic hyperventilation, threshold load (TL) is independent of flow rate. Also, TL enhances the velocity of inspiratory muscle contraction, shortening inspiratory time and increasing time for exhalation and relaxation. However, at high loads decrease in T_i for a given P_{di} $P_{di\ max}$ reduces T_i/T_{tot} thereby reducing P_{di}, which may be the most important training variable. Despite improvement in respiratory muscle strength and endurance (79,80), with relief in breathlessness in some patients (67–69), IMT may not result in enhanced exercise performance (79).

TRAINING OF PERIPHERAL MUSCLES

Strength training (ST)

ST is obtained by additional weights to lower and upper limb movement. The importance of peripheral skeletal muscle dysfunction in the impairment of exercise capacity and LE in patients with COPD was suggested by Killian and colleagues (81,82). Training of peripheral muscle strength has been shown to improve maximal muscle strength, exercise endurance capacity and QoL but not maximal exercise capacity (83,84). In healthy subjects, strength training may (85) or may not (86) enhance the effect of endurance training. In patients with COPD, the addition of strength training to endurance training has no additional effect on exercise performance and QoL (87). However, in patients with muscle weakness the combination of strength with endurance appears to

Table I. Summary of scientific evidence grades for the described techniques

Program contents	Recommendations	Grade
Lower extremity training	Lower extremity training improves exercise tolerance and is recommended as a part of pulmonary rehabilitation	A
Upper extremity training	Strength and endurance training improves arm function; arm exercises should be included in pulmonary rehabilitation	B
Ventilatory muscle training	Is not an essential component of pulmonary rehabilitation	B
Oxygen administration	Does not enhance rehabilitation outcomes	D
Breathing retraining	No advantages.	D
Respiratory muscle rest	Can enhance skeletal muscle training	C

Modified from refs. (70, 102).

increase peripheral muscle strength, exercise performance and QoL (48).

Endurance arm exercise training (AET)

AET involves a larger muscle mass working at moderate intensity for a longer period of time. For equal work rates, ventilation and oxygen consumption are generally higher for arm than for leg exercise (88,89). This is probably due to a lower mechanic efficiency of the arm muscle because more static work is needed to stabilize trunk and shoulder. It likely follows an earlier onset of anaerobic metabolism for the arms than for the legs. The effect of unsupported arm exercise (UAET) on respiratory system increases by increasing arm loading (90). In severely obstructed patients, AET is associated with dyssynchronous breathing and is terminated because of severe dyspnea, this not being observed with the same patients performing more intense leg (cycle) exercise, with a higher V_{O_2}, heart rate and exercise duration (91). The reason for dyssynchronous breathing with AET was thought to be due to a decreased contribution of RC and accessory muscles to ventilation overtaxing the diaphragm and leading to its earlier fatigue. Several lines of evidence indicate that unsupported AET increases V_{O_2}, CO_2 output (V_{CO_2}), end inspiratory gastric pressure (P_{gai}) and both end expiratory pleural (P_{ese}) and gastric (P_{gae}) pressures in patients with CAO (92). Compared to UAET, supported AET (SAET) decreases P_{gai} and P_{esi} pressures and P_{gae} in most of the COPD patients again indicating that a greater part of VE during UAET is shifted from RC inspiratory muscles to both the diaphragm and the expiratory muscles.

Comprehensive pulmonary rehabilitation including arm exercise decreases metabolic and ventilatory requirement for AET (93). The reduction of V_{O_2} during arm activity which results from such training might be expected to improve dyspnea (1). Upper extremity (UE) training program improves specific UE performances (38,93–95) but not activities simulating daily living (38,94) or walking test (95).

UNLOADING THE RESPIRATORY MUSCLES

Maltais *et al*. (96) showed that 11 cmH_2O of inspiratory pressure support reduces both inspiratory effort and dyspnea in severe CAO patients performing constant work load bicycle exercise. In particular, the inverse relationship between improvement in dyspnea and decrease in pressure–time integral of both inspiratory muscles and the diaphragm, i.e., decrease in inspiratory effort was evident. Furthermore, there was no further change in EELV with addition of PS compared with control exercise. The authors maintained that, unlike continuous positive airway pressure (CPAP), the efficacy of inspiratory support do not necessarily depend on either the prevailing level of intrinsic positive end expiratory pressure ($PEEP_i$) or the presence of expiratory FL.

O'Donnell *et al*. (97) were able to show that CPAP decreased dyspnea in exercising patients with CAO. They postulated that unloading the respiratory muscles resulted in a decreased central respiratory output and thereby a decreased inspiratory effort, in as much as, in exercising patients trans-pulmonary pressure promotes airway compression thus contributing to dyspnea. The application of 4 cmH_2O positive end expiratory pressure (PEEP) contributed to dyspnea relief by attenuating dynamic compression (97). In two recent papers, Harms *et al*. (98,99) have shown that unloading the respiratory muscles with proportional assist ventilation during strenuous exercise in cyclists reduces oxygen uptake and the perception of both breathlessness and leg discomfort, indicating that work of breathing significantly influences exercise performance. The effect of the normal respiratory muscle load on exercise performance in trained cyclists may be due to the associated reduction in leg blood flow which increases both leg fatigue and the intensity with which leg effort and respiratory muscle effort are perceived. This also explains the difficulty of discriminating between the two sensations. The link between respiratory work and exercise performance is likely to be due to a vasoconstrictor effect from the diaphragm to the limb muscle vasculature. This

occurs during heavy exercise with sustained work of breathing and cardiac output limited in its ability to distribute flow adequately to both respiratory and locomotor muscles. The same may happen in conditions of moderate exercise when cardiac output is abnormally low, likely to occur in exercising patients with severe COPD. Recently, Garrod *et al*. (100) have shown that the addition of non-invasive pressure positive ventilation (NPPV) to an exercise training program in severe COPD results in a significant improvement in mean shuttle walk test. At variance, Bianchi *et al*. (101) have recently shown that proportional assist ventilation during training sessions included in a multidisciplinary PRP is not well tolerated by all patients and gave no additional physiological benefit in comparison with exercise training alone (Table 1).

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